

### Remarks

Claims 8-11, 13, 15-19 and 21-29 are pending and claims 21-29 are currently under examination. Claims 21, 23 and 25-28 have been amended, claims 22, 24 and 29 have been canceled. Support for the claim amendments and new claims can be found throughout the Specification and the claims as originally filed. No new matter has been added.

Exemplary support for the amendments to claim 21 and 28 can be found at page 16, lines 20-22 and page 20, lines 7-10, and to claim 23 can be found at page 16, lines 10-11, and to claim 25 can be found at page 16, line 19, to page 17, line 7.

Amendments of claims should in no way be construed as acquiescence to any of the Examiner's rejections. The amendments to the claims are being made solely to expedite prosecution of the present application. Applicants reserve the right to further prosecute the same or similar claims in the instant or in a subsequent related patent application.

### Objection to the Specification

Applicants have amended the Abstract as suggested by the Examiner. Accordingly, reconsideration and withdrawal of this objection is respectfully requested.

### Rejection of Claims 21-29 under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 21-29 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. As Applicants have herein canceled claims 22 and 29, the rejection of these claims is moot. Applicants respectfully traverse this rejection as applied to the non-canceled claims.

Applicants herein have amended claims 21 and 28 to more clearly point out that subpart (b) comprises a bead coated with an extracellular matrix protein. It is believed that the claim amendments obviate all grounds for the present rejection. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

**Rejection of Claims 21-29 under 35 U.S.C. § 103(a)**

The Examiner has rejected claims 21-29 under 35 U.S.C. § 103(a) as being unpatentable over Mitaka et al. (Hepatology 1999) in view of Naughton et al. (US # 5,624,840) and Vacanti et al (US # 5,759,830) and Matsui et al. (US # 5,298,615). Applicants respectfully traverse this rejection. As Applicants have herein canceled claims 22, 24 and 29, the rejection of these claims is moot.

According to the Examiner, one skilled in the art could co-culture the hepatic and nonparenchymal cells together, as disclosed in Mitaka et al., on the three-dimensional matrix, as suggested by Naughton et al. and Vacanti et al., to obtain function of the matrix or scaffold in producing tissue having liver formation. Further, the Examiner states it would have been obvious to provide the matrix or scaffold in the form of polystyrene, as suggested by Matsui et al.

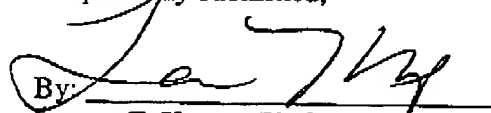
Applicants herein have amended claims 21 and 28 to recite that hepatocyte and nonparenchymal cells are co-cultured in the presence of the epidermal growth factor on beads that are coated with extracellular matrix protein. Neither the epidermal growth factor and/or the beads that are coated with extracellular matrix protein are taught or suggested in Mitaka et al., Naughton et al., Vacanti et al and Matsui et al., or any other prior art of which we are aware. It

is believed that the claim amendments obviate all grounds for the present rejection. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

**Conclusion**

In view of the above remarks and the amendments to the claims, it is believed that this application is in condition for allowance. If a telephone conversation with Applicant's Agent would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 832-1000.

Respectfully submitted,

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Dated: December 18, 2003